CORONARY ARTERY DISEASE

Adverse prognosis associated with the metabolic syndrome in established coronary artery disease: data from the EUROPA trial

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Objective: To assess the prevalence of metabolic syndrome, and its effect on cardiovascular morbidity and mortality in patients with established coronary disease and to explore the inter-relationships between metabolic syndrome, diabetes, obesity and cardiovascular risk.

Methods: The presence of metabolic syndrome was determined in 8397 patients with stable coronary disease from the European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease, with mean follow-up of 4.2 years. Metabolic syndrome was defined using a modified version of the National Cholesterol Education Programme criteria.

Results: Metabolic syndrome was present in 1964/8397 (23.4%) of the population and significantly predicted outcome; relative risk (RR) of cardiovascular mortality = 1.82 (95% CI 1.40 to 2.39); and fatal and non-fatal myocardial infarction RR = 1.50 (95% CI 1.24 to 1.80). The association with adverse outcomes remained significant after adjustment, RR of cardiovascular mortality after adjustment for conventional risks and diabetes = 1.39 (95% CI 1.03 to 1.86). In comparison with normal weight subjects without diabetes or metabolic syndrome, normal weight dysmetabolic subjects (with either diabetes or metabolic syndrome) were at substantially increased risk of cardiovascular death (RR = 4.05 (95% CI 2.38 to 6.89)). The relative risks of cardiovascular death for overweight and obese patients with dysmetabolic status were nominally lower (RR = 3.01 (95% CI 1.94 to 4.69) and RR = 2.35 (95% CI 1.50 to 3.68), respectively).

Conclusions: Metabolic syndrome is associated with adverse cardiovascular outcome, independently of its associations with diabetes and obesity. A metabolic profile should form part of the risk assessment in all patients with coronary disease, not just those who are obese.

The metabolic syndrome is a constellation of cardiovascular risk factors centred around obesity, abnormal glucose metabolism, hypertension and dyslipidaemia. These risk factors tend to cluster together in subjects, and when they do, substantially increase the risk of the development of cardiovascular disease.[1 2]

The prevalence of the metabolic syndrome is increasing,[3–5] coincident with increasing levels of obesity related to sedentary lifestyles and malnutrition.[6] However, it is becoming clear that other factors, such as the distribution of body fat, whether visceral or subcutaneous, modify the relationship between weight and metabolic status.[7–9]

The metabolic syndrome portends the onset of diabetes[11] and is associated with intermediate risk for the development of cardiovascular disease relative to diabetes in population-based studies.[12] Furthermore, it has been shown to be predictive of cardiovascular mortality and major cardiovascular events.[10 13–16]

Despite a growing body of data about the prevalence and prognostic importance of metabolic syndrome in the general population and asymptomatic high-risk populations, the prevalence and clinical consequences of the metabolic syndrome in patients with established cardiovascular disease are less well defined.

We sought to determine the prevalence of the metabolic syndrome in a population with stable coronary disease, to assess its effect on major cardiovascular events in this group, and to explore the complex relationships between obesity, the metabolic syndrome and diabetes and their impact on cardiovascular events.

PATIENTS AND METHODS

Population

The presence or absence of the metabolic syndrome was determined in patients with known coronary disease from the European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease (EUROPA), a placebo-controlled trial of the effect of perindopril on cardiovascular outcome. The principal results and methods of the EUROPA trial have previously been published.[17] Briefly, men and women >18 years of age, with objective evidence of coronary disease, but without clinical heart failure were enrolled in the study. Previous myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, or angiographically documented coronary stenosis >70% were accepted as objective evidence of coronary disease, or a positive stress test in symptomatic men. The main exclusion criteria were clinical evidence of heart failure, planned revascularisation, hypotension (sitting systolic blood pressure of <110 mm Hg) or uncontrolled hypertension (systolic blood pressure >180 mm Hg or diastolic blood pressure of >100 mm Hg, or both), recent (<1 month) use of ACE inhibitor or angiotensin receptor blocking treatment, renal insufficiency (creatinine >150 μmol/l) or serum potassium >5.5 mmol/l. Each institution's review

Abbreviations: BMI, body mass index; EUROPA, European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease; HDL, high-density lipoprotein; MI, myocardial infarction; NCEP, National Cholesterol Education Program; RR, relative risk

Table 1 Baseline demographic and clinical characteristics according to individual metabolic subgroups

Characteristics	Metabolic syndrome absent			Metabolic syndrome present		
	All (n = 6433)	Without diabetes (n = 5712)	With diabetes (n = 721)	All (n = 1964)	Without diabetes (n = 1183)	With diabetes (n = 781)
Age (years), mean (SD)	60 (9)	60 (9)	63 (8)	59 (9)	57 (9)	61 (9)
Male	87.1	87.1	87.2	79.6	81.2	77.1
Current smoker	14.7	15.1	12.1	14.2	15.7	11.9
Hypertension	29.3	25.4	36.9	37.7	35.0	41.9
Hyperlipidaemia	61.9	62.3	58.7	63.4	64.0	62.6
Prior MI	65.8	65.9	64.8	68.2	68.1	68.2
Prior CABG	30.4	29.0	33.4	26.6	24.3	30.2
Prior PTCA	29.5	30.8	27.3	26.3	27.0	25.1
Prior TIA/CVA	3.3	2.9	5.8	4.1	3.3	5.2
PVD	9.3	7.0	12.6	7.6	7.0	12.7

Results are shown as percentages unless stated otherwise.
MI, myocardial infarction; CABG, coronary artery bypass graft; PTCA, percutaneous transluminal coronary angioplasty; TIA, transient ischaemic attack; CVA, cerebrovascular accident; PVD, peripheral vascular disease.

board or ethics committee reviewed the protocol and all participants provided informed consent.

Of the 12 218 randomised patients in the original study, 1502 had known diabetes at baseline, either from self-report or patient records and a further 6895 had a fasting glucose taken as part of the study. Thus a total of 8397 patients in whom diabetic or glycaemic status was known were included in this analysis. The metabolic syndrome was defined using a modified version of the National Cholesterol Education Program (NCEP) criteria.[18] The metabolic syndrome was deemed present if at least three of the following were present: blood pressure >130/85 mm Hg or receiving antihypertensive drug treatment; high-density lipoprotein (HDL) <1.0 mmol/l (male) and <1.3 mmol/l (female); body mass index (BMI) >30 kg/m^2; fasting plasma glucose >6.1 mmol/l or the presence of known diabetes.

Biochemical measurements and follow-up

Plasma total cholesterol, low-density lipoprotein cholesterol and HDL cholesterol were measured locally at baseline. Fasting plasma glucose in patients without known diabetes was also measured locally. Patients were followed up at 3, 6 and 12 months and every 6 months thereafter for an average of 4.2 years. Cardiovascular mortality was adjudicated by a central critical event committee on the basis of necropsy results if available, or documentary evidence from medical records of the immediate clinical history before death. All end points were included in analysis only if confirmed by the independent critical event committee.

Statistical analysis

Data are presented as mean (SD) for continuous variables and number (%) of subjects for categorical variables. Incidence rates are presented as number of events per 1000 patient-years. Cox proportional hazard models were used to determine the univariate risk associated with the metabolic syndrome for the combined end point of cardiovascular death, myocardial infarction (MI) or cardiac arrest, the primary end point used in the EUROPA study, and also cardiovascular mortality, total mortality, fatal and non-fatal myocardial infarction, stroke and admission to hospital for heart failure. The effects of each of the component risks of the metabolic syndrome on the combination end point cardiovascular death and MI and resuscitated cardiac arrest were examined in univariate and multivariable models. Multivariable proportional hazard models were employed to serially adjust the risks of cardiovascular and total mortality, MI and the combination end point for conventional risk factors and gender, and finally, for each of the constituent risks for the metabolic syndrome individually. Total cholesterol, age and current smoking status were considered as conventional risks. Interaction between the presence or absence of known diabetes and the presence or absence of the metabolic syndrome was investigated within the proportional hazards models. Statistical analysis was undertaken with the assistance of Cardialysis, the Netherlands.

To explore the relationship between weight, the metabolic syndrome and cardiovascular risk the cumulative probabilities of cardiovascular death according to weight and metabolic

Table 2 Prevalence of individual constituent risks of the metabolic syndrome according to individual metabolic subgroups

Constituents	Overall (n = 8397)	Metabolic syndrome absent		Metabolic syndrome present	
		Without diabetes (n = 5712)	With diabetes (n = 721)	Without diabetes (n = 1183)	With diabetes (n = 781)
Diabetes	17.9	0	100	0	100
Fasting glucose >6.1 (in absence of diabetes)	22.0	17.0	0	73.9	0
Hypertension (BP >130/85 mm Hg or receiving antihypertensive drug treatment)	91.7	90.0	86.5	99.0	98.5
HDL <1.0 mmol/l (male) or <1.3 mmol/l (female)	31.9	20.4	4.4	79.2	69.9
Obesity (BMI >30 kg/m^2)	21.8	10.1	1.2	66.4	58.7

Results are shown as percentages.
BP, blood pressure; HDL, high-density lipoprotein; BMI, body mass index.

Table 3 Blood pressure and lipid levels at baseline and at 4 years

	Baseline		4 Years	
	No met syn	Met syn	No met syn	Met syn
Systolic BP (mm Hg)	137 (15)	139 (16)	131 (16)	134 (16)
Diastolic BP (mm Hg)	82 (8)	83 (8)	78 (9)	79 (8)
Cholesterol (mmol/l)	5.4 (1)	5.4 (1)	–	–
LDL (mmol/l)	3.4 (1)	3.4 (1)	–	–
HDL (mmol/l)	1.3 (0.5)	1.0 (0.3)	–	–
Use of lipid lowering drugs (%)	54	55	70	71
Antihypertensive drugs (n)	1.0 (0.6)	1.2 (0.6)	1.1 (0.7)	1.3 (0.7)

Results are shown as mean (SD) unless stated otherwise.
BP, blood pressure; LDL, low-density lipoprotein; HDL, high-density lipoprotein.

status were examined. For this purpose the population was stratified into normal weight, overweight or obese patients according to the BMI, with a BMI <25 kg/m^2 considered normal weight, BMI 25–30 kg/m^2 considered overweight and BMI >30 kg/m^2 considered obese. Patients were then categorised as having dysmetabolic status if they had either diabetes or the metabolic syndrome, or as having normal metabolic status if not. The relative risk of cardiovascular death associated with each category was then estimated using a proportional hazards model, with normal weight, normal metabolic status as the reference. A further analysis was undertaken using a fourth weight category, underweight (BMI <20 kg/m^2), to ascertain if the recognised association between underweight and adverse outcome had a major influence on these results.

The relative risks of cardiovascular death associated with increasing numbers of constituent risks of the metabolic syndrome compared with no constituent risks were also calculated.

RESULTS

Population

The mean (SD) age of the 8397 patients in whom the presence or absence of the metabolic syndrome was ascertained was 60 (9) years, and 87% were male. Two thirds (66%) had had a previous MI. Prior revascularisation had been performed in 55%, 29% having had previous bypass surgery and 29% previous percutaneous revascularisation. Coronary angiography had demonstrated significant stenosis in at least one coronary artery in 60%. A definite prior MI, significant coronary artery disease documented at angiography or prior revascularisation accounted for >96% of patients, with only a small proportion included on the basis of a history of angina and positive non-invasive test. The metabolic syndrome, as defined by the modified NCEP definition described was detected in 23.4% of the population. Diabetes with the metabolic syndrome was present in 9%, diabetes without the metabolic syndrome in 9% and the metabolic syndrome without diabetes in 14%. Table 1 describes the baseline characteristics of the group according to metabolic status. Patients with the metabolic syndrome were younger, more of them were female, had higher prevalence of prior MI and peripheral vascular disease and had less revascularisation before inclusion, and each of these differences was significant. Significance of the difference in history of hypertension was not assessed, as hypertension was one of the selection criteria for inclusion in the metabolic syndrome group. Table 2 shows the prevalence of each of the constituent risks of the metabolic syndrome according to metabolic subgroup. Table 3 shows blood pressure and lipid treatment at baseline and at 4 years.

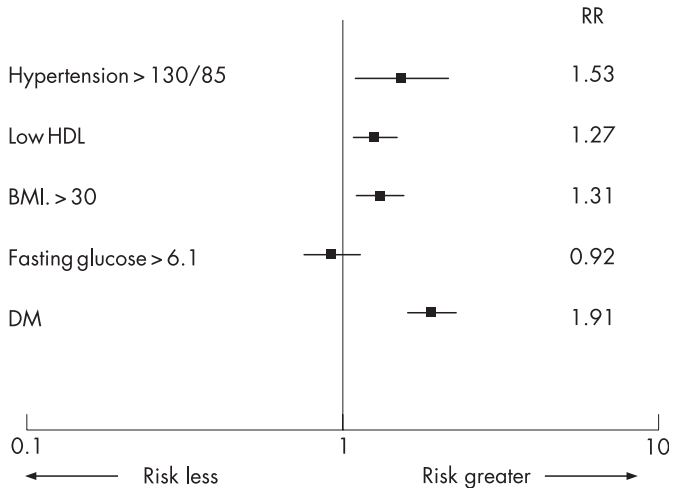


Figure 1 Multivariable relative risk (RR) of cardiovascular death, myocardial infarction or cardiac arrest for each of the constituent risks of the metabolic syndrome (including adjustment for age, gender, and total cholesterol). HDL, high-density lipoprotein; BMI, body mass index; DM, diabetes mellitus.

Effect of the metabolic syndrome on cardiovascular outcomes

Over the 4-year follow-up period the metabolic syndrome was associated with significantly increased risk of the combined end point of cardiovascular death, MI and resuscitated cardiac arrest, the primary end point of the EUROPA trial, relative risk (RR) = 1.55 (95% CI 1.32 to 1.82), $p<0.001$. The risk of individual end points was also significantly increased, including cardiovascular mortality, RR = 1.82 (95% CI 1.40 to 2.39), $p<0.001$; total mortality, RR = 1.54 (95% CI 1.24 to 1.91), $p<0.001$; fatal and non-fatal MI, RR = 1.50 (95% CI 1.24 to 1.80), $p<0.001$; and admission to hospital for heart failure, RR = 1.64 (95% CI 1.14 to 2.38), $p = 0.008$. With the exception of impaired fasting glycaemia in the absence of diabetes, each of the components of the metabolic syndrome (diabetes, hypertension >130/85 mm Hg, obesity, or low HDL) were significant predictors of cardiovascular events in this population independently of each other, and after adjustment for conventional risk factors (fig 1). The presence of diabetes was associated with the greatest increase in risk.

Adjustment for gender and conventional risk factors, including age, total cholesterol and smoking status did not reduce the significant adverse effect of the metabolic syndrome on the combined end point of cardiovascular death, MI and resuscitated cardiac arrest, individual components of this end point, or total mortality (table 4). Furthermore, although the association between the metabolic syndrome and total mortality was no longer significant after adjustment for the presence of diabetes, the adverse effects of the metabolic syndrome on the major cardiovascular end points remained significant after

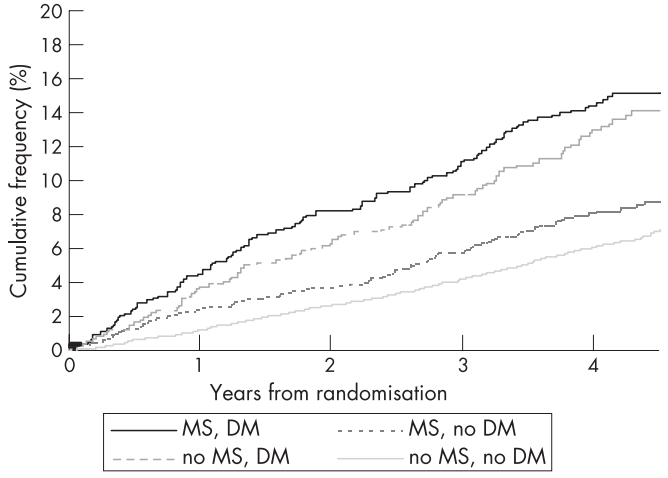
Table 4 Multiple adjusted relative risks of selected end points associated with the presence of the metabolic syndrome

Risk associated with metabolic syndrome	Cardiovascular mortality RR (95% CI)	Total mortality RR (95% CI)	Fatal and non-fatal MI RR (95% CI)	Cardiovascular death, MI, or cardiac arrest RR (95% CI)
Adjusted for age, sex, total cholesterol and smoking status	2.11 (1.61 to 2.77)	1.80 (1.44 to 2.24)	1.52 (1.26 to 1.84)	1.63 (1.39 to 1.92)
Additionally adjusted for the presence of:				
Diabetes	1.39 (1.03 to 1.86)	1.16 (0.91 to 1.47)	1.33 (1.09 to 1.64)	1.33 (1.11 to 1.58)
BP >130/85 mm Hg or treated hypertension	1.99 (1.52 to 2.62)	1.73 (1.39 to 2.17)	1.48 (1.22 to 1.80)	1.59 (1.34 to 1.87)
Low HDL <1.0 mmol/l (men) <1.3 mmol/l (women)	2.22 (1.60 to 3.08)	1.88 (1.44 to 2.46)	1.37 (1.10 to 1.73)	1.56 (1.29 to 1.90)
Obesity (BMI >30 kg/m^2)	1.96 (1.40 to 2.73)	1.74(1.33 to 2.28)	1.37 (1.08 to 1.73)	1.48 (1.21 to 1.81)
Fasting glucose >6.1 mmol/l (in absence of diabetes)	2.53 (1.91 to 3.36)	2.15 (1.71 to 2.71)	1.70 (1.39 to 2.08)	1.84 (1.55 to 2.19)

RR, relative risk; MI, myocardial infarction; BP, blood pressure; HDL, high-density lipoprotein; BMI, body mass index.

additional adjustment for diabetes (table 4). In particular, the effect of the metabolic syndrome on cardiovascular mortality and on non-fatal MI was independent of the effect of diabetes. Diabetes remained a strong and independent predictor of cardiovascular mortality RR = 3.32 (95% CI 2.51 to 4.38), p<0.001; total mortality RR = 3.48 (95% CI 2.79 to 3.35), p<0.001; fatal and non-fatal MI RR = 1.51 (95% CI 1.22 to 1.88), p<0.001; and the combination end point of cardiovascular death, MI or cardiac arrest RR = 1.89 (95% CI 1.59 to 2.26), p<0.001, after adjustment for the effects of the metabolic syndrome and other risks. The effects on cardiovascular outcome of diabetes and the metabolic syndrome did not interact significantly, p = 0.47 for the combined end point of cardiovascular death, MI or cardiac arrest.

Figure 2 illustrates clearly that the presence of the metabolic syndrome was associated with incremental risk in the diabetic population, showing the cumulative probability of cardiovascular death, MI and resuscitated cardiac arrest according to the presence or absence of diabetes and the metabolic syndrome. The metabolic syndrome also remained a significant predictor of all of the major end points after additional adjustment for each of the remaining component risks of the metabolic syndrome individually (table 4).



	Randomisation	1 year	2 years	3 years	4 years
MS, DM	781	743	710	682	509
no MS, DM	721	692	665	631	453
MS, no DM	1183	1154	1139	1108	928
no MS, no DM	5712	5644	5557	5435	4433

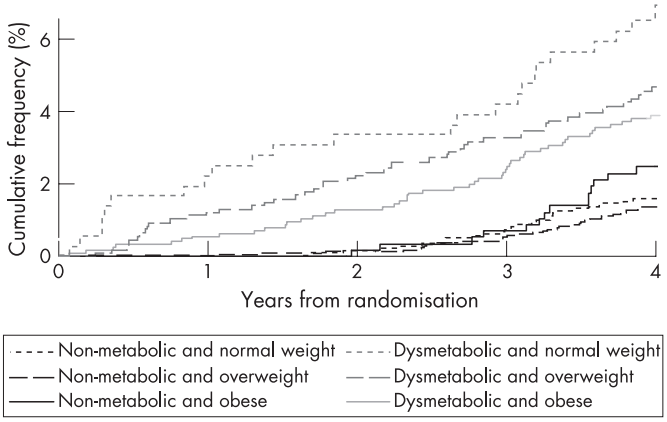
Figure 2 Cumulative probability of cardiovascular mortality, myocardial infarction or cardiac arrest associated with metabolic subgroups. MS, metabolic syndrome; DM, diabetes mellitus.

Effect of perindopril

The relative risk of the primary end point associated with the metabolic syndrome in the perindopril treated population was 1.68 (95% CI 1.32 to 2.13). The effect of perindopril in reducing cardiovascular death, MI or cardiac arrest (the primary end point of the EUROPA study) was not significantly different in patients with or without the metabolic syndrome, RR = 13% (95% CI to 13% to 34%) in the metabolic syndrome subgroup, and RR = 25% (95% CI 10% to 37%) in the population without the metabolic syndrome. Despite the apparent, although non-significantly, lower relative risk reduction, the absolute rate difference was similar, 4 per 1000 patient-years (metabolic syndrome) and 5 per 1000 patient-years (no metabolic syndrome) because of the higher event rate in the metabolic syndrome population.

Weight and the metabolic syndrome

To investigate the relationship between the metabolic syndrome, BMI and cardiovascular risk the cumulative probabilities of cardiovascular death were plotted for those with and those without dysmetabolic features, stratified into normal weight, overweight and obese categories (fig 3). As expected, patients with diabetes or the metabolic syndrome (dysmetabolic) fared worse than those without. But within this subgroup the probability of cardiovascular death was greater among patients with normal weight than those who were



Patients at risk	Randomisation	1 year	2 years	3 years	4 years
Non-metabolic and normal weight	1644	1644	1640	1616	1325
Dysmetabolic and normal weight	357	347	341	336	243
Non-metabolic and overweight	3489	3489	3484	3449	2864
Dysmetabolic and overweight	1074	1060	1040	1014	809
Non-metabolic and obese	579	579	576	572	458
Dysmetabolic and obese	1254	1244	1232	1208	988

Figure 3 Cumulative probability of cardiovascular death according to weight and metabolic status.

Table 5 Relative risk of cardiovascular death according to body mass index (BMI) and metabolic status

BMI and metabolic status	CV death (%)	Events per 1000 patient-years	RR (95% CI)	p Value
Normal weight, not dysmetabolic	1.8	4.3	1.0	
Overweight, not dysmetabolic	1.6	3.8	0.89 (0.57 to 1.38)	0.59
Obese, not dysmetabolic	2.6	6.1	1.42 9 (0.76 to 2.63)	0.27
Normal weight, dysmetabolic	7.0	17.2	4.05 (2.38 to 6.89)	<0.001
Overweight, dysmetabolic	5.3	12.8	3.01 (1.94 to 4.69)	<0.001
Obese, dysmetabolic	4.2	10	2.35 (1.50 to 3.68)	<0.001

Normal weight: BMI <25; overweight: BMI 25–30; obese: BMI >30.
Dysmetabolic, diabetic or with metabolic syndrome (three of the National Cholesterol Education Program criteria[18]).

overweight or obese. Table 5 shows the risks of cardiovascular death for each subgroup relative to the normal weight population with normal metabolic status. Sensitivity analysis separating those who were underweight from those of normal weight and stratifying by metabolic status demonstrated a similar pattern. Patients of dysmetabolic status and normal weight remained at greater relative risk than those who were overweight or obese.

Number of component risks

Examination of the risk of cardiovascular death associated with increasing numbers of component risks of the metabolic syndrome showed a cumulative increase in risk with increasing numbers of component risks of the metabolic syndrome. The relative risk associated with just one of the component risks versus none did not meet statistical significance, RR = 1.80 (0.56 to 5.78), p = 0.32. However, the presence of two component risks compared with those with no features of the metabolic syndrome increased the risk of cardiovascular death significantly, RR = 3.78 (1.20 to 11.92), p = 0.02, even after adjustment for age, gender, total cholesterol and current smoking status, and the risk increased as the number of risks present increased. The relative risk of cardiovascular death associated with three of the component parts of the metabolic syndrome was 5.57 (1.737 to 17.84), p = 0.004, and with four component risks was 7.66 (2.24 to 26.26), p<0.001.

DISCUSSION

This study provides valuable information about the impact of the metabolic syndrome in patients with coronary disease. Further strengths include its size, the collection of long-term follow-up data, and the assessment of the effects of metabolic syndrome relative to diabetes. There are limitations to the data. Fasting glucose was not measured at baseline in all subjects, introducing a degree of selection bias. The prevalence of known diabetes may be overestimated, as all known diabetic subjects were included, although only 67% of the population not known to have diabetes were screened. Only four of the five NCEP standard criteria for definition of the metabolic syndrome were captured on the database. Triglyceride levels were not. However, as triglyceride levels and HDL levels are closely associated and both are measures of lipoprotein abnormality, it was considered reasonable to just use one lipoprotein abnormality index when all the other indices of the metabolic syndrome were available. The WHO criteria for the metabolic syndrome use either high triglycerides or low HDL as a marker of dyslipidaemia. The WHO cut-off point for obesity, BMI >30 kg/m^2, was used as a surrogate for increased waist circumference. Analysis of data from the NHANES III survey showed that 97% of patients identified as having the metabolic syndrome using BMI would have been identified if waist circumference had been used.[19]

The study identifies the metabolic syndrome as a relatively common condition in patients with stable coronary disease, affecting almost a quarter of this European population (23.4%), consistent with other European reports.[20 21] The results indicate similar or even higher levels of hypertension (92%) as in the REACH registry (82%).[22] The prevalence of hypercholesterolaemia (62%), diabetes (18%) and obesity (21%) were also lower, compared with 72%, 44% and 27%, respectively, in REACH. The use of lipid lowering treatment had increased during the course of the trial in EUROPA, although it remained lower than in the REACH registry patients with known coronary disease. Some of these differences reflect altered definitions and temporal trends in the application of more intensive treatment during the time between the start of the EUROPA trial and recruitment to the REACH registry. From this study it is also apparent that in a large population with established coronary disease the metabolic syndrome is associated with clinically important and statistically significant increases in the rates of cardiovascular death (a greater than twofold increase), and MI (~ 50% increase), even after adjustment for conventional risks. The effect of the metabolic syndrome on cardiovascular events was independent of its association with diabetes, and the risks associated with diabetes and the metabolic syndrome incremental to each other.

Although obesity is a significant predictor of adverse cardiovascular events independent of conventional risks, its effect appears to be mediated through its association with the metabolic syndrome or dysmetabolic status. When stratified by BMI and dysmetabolic status, the effects of increasing weight and dysmetabolic status diverge, as previously observed in the considerably smaller, female population in the WISE study.[23] Several factors may shed some light on this apparently counterintuitive result. Although well validated as an indicator of increased cardiovascular mortality in population-based studies, BMI is a crude measure of propensity to insulin resistance and the metabolic syndrome. The distribution of body fat rather than weight itself is a crucial factor in predicting the occurrence of the metabolic syndrome,[7] with visceral and intramuscular adiposity more closely associated with metabolic abnormalities than BMI.[8 9 24–26] Furthermore, dysmetabolic status is (inversely) related cardiovascular fitness, which is a marker of improved prognosis even with increased BMI.[27 28]

The clinical implications of these findings occur at the level of diagnosis and therapeutic intervention. The metabolic syndrome is associated with increased cardiovascular risk independently of conventional risk factors, and has been shown to give prognostic information additional to that provided by the Framingham risk equation.[20] However, even conventional risk factors are still not optimally measured in clinical practice.[29 30] Awareness of the prognostic implications of the metabolic syndrome in addition to conventional risk factors should prompt more complete risk factor evaluation to refine risk prediction for individual patients.[31 32] A more refined approach to risk prediction also offers greater therapeutic potential.[31 32]

Multifactorial risk factor intervention has been shown to be highly successful in achieving reduction in cardiovascular event rates in the diabetic population,[33] and holds promise for those with the metabolic syndrome. Intensive lipid lowering and blood pressure control can improve the prognosis in patients with the metabolic syndrome.[34 35] Meanwhile exercise and lifestyle modification programmes in patients with the metabolic syndrome have shown positive results in reducing individual risk factors[36] and reducing the development of diabetes.[37 38] In the future, insulin sensitising agents may be used to avert or delay the onset of diabetes in these patients, and new weight reducing agents may be used to positively modify metabolic abnormalities in parallel with weight reduction[39] in a manner which mechanical methods cannot.[40]

CONCLUSION

The metabolic syndrome affects a clinically important proportion of patients with coronary disease and is associated with an adverse prognosis. The risk conferred is less than, but incremental to, that associated with overt diabetes. The metabolic syndrome is associated with increased cardiovascular risk independently of obesity, but the effect of obesity on cardiovascular outcome is not independent of metabolic status. Those with normal weight and dysmetabolic status appear at particularly high risk of cardiovascular events. Comprehensive risk assessment including determination of metabolic status should be carried out in all patients to optimise risk prediction and allow all therapeutic avenues to be pursued.

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